

AGING AND BONE QUALITY

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P.T.

Keywords:

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National Institute of Arthritis and Musculoskeletal and Skin Diseases

PURPOSE

The National Institute on Aging (NIA) and National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) invite research applications to elucidate the nature and consequences of age-related changes in bone quality and the relationship of these changes to enhanced bone fragility and susceptibility to osteoporotic fractures. Factors that contribute to bone quality include architecture, density and mechanical strength.

HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This Program Announcement (PA), Aging and Bone Quality, addresses the priority area of osteoporosis. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

ELIGIBILITY REQUIREMENTS

Applications may be submitted by foreign and domestic, non-profit and for-profit organizations, private and public such as colleges, universities, laboratories, units of state and local governments, and eligible agencies of the Federal government. Foreign institutions are not eligible for First Independent Research Support and Transition (FIRST) awards (R29). Applications from minorities and women are encouraged.

MECHANISM OF SUPPORT

Support for this program will be by the research project grant (R01) and the FIRST (R29) award.

RESEARCH OBJECTIVES

Background

The progressive loss of bone with age very commonly leads to osteoporosis, a condition characterized by increased skeletal fragility and susceptibility to fracture. Osteoporosis and its consequences are a significant cause of frailty, morbidity, and even mortality. However, while in older individuals reduced bone mass is important both in contributing to and predicting an enhanced risk of fracture, low bone mass alone is not a sufficient explanation for osteoporotic fractures. This is exemplified by the substantial overlap in bone density between normal individuals and patients who sustain hip and other osteoporotic fractures. A new perspective is needed that broadens the conceptual basis of skeletal integrity to include in addition to bone mass, qualitative factors that may impact on bone strength such as geometry, macro and micro-structural organization, distribution of material within bone, biochemical composition, and the burden of unrepaired microdamage.

An NIA Workshop on Aging and Bone Quality, held September 3-4, 1992, underscored the need to study bone quality and identified promising new areas of research, which can be found in the workshop Proceedings in *Calcified Tissue International*, Supplement 1, (53), 1993. This PA reflects the priority areas that were identified at the workshop.

This PA is directed towards: (1) stimulating research aimed at elucidating age-related mechanisms that influence the development and/or course of osteoporosis and (2) developing strategies aimed at preventing or lessening the burden of osteoporosis-related fractures in older individuals. Specifically, this PA seeks applications for basic and clinical research to identify and evaluate the effects of age on factors related to bone quality and/or strategies to modify the impact of these factors on skeletal fragility and increased fracture susceptibility. Topics of interest include, but are not limited to:

- o Age-related changes in architecture, mechanical properties, and strength of bone
- o Evaluation of changes in bone matrix and mineralization and their impact on strength and resistance to microdamage
- o Assessment of the consequences of age on the accumulation of cortical and trabecular microdamage and their relationship to bone strength and fracture biomechanics
- o Age-related changes in the detection of microdamage and activation, and initiation of the remodelling and repair processes in bone

- o Determination of age- and disease-related changes in biochemical, cellular, and structural factors affecting bone quality
- o Elucidation of the role and function of osteocytes and bone lining cells in bone metabolism
- o The nature of changes in osteocyte viability and function with age and the effect of these changes on the structural and mechanical properties of bone
- o Development of model systems that reflect normal physical and physiological aspects related to functional loading and responses to loading in aged bone
- o Development and application of techniques such as histomorphometry, ultrasound, NMR, and QCT to evaluate changes in architecture, bone strength and fracture susceptibility

STUDY POPULATIONS

INCLUSION OF WOMEN AND MINORITIES IN RESEARCH INVOLVING HUMAN SUBJECTS

Awards for research involving human subjects must follow the "NIH Guidelines On the Inclusion of Women and Minorities as Subjects in Clinical Research." See the RFA for details.

APPLICATION PROCEDURES

Applications are to be submitted on the application form PHS 398 (rev. 9/91) available at most institutional offices of sponsored research and from the Office of Grants Information, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone 301-435-0714. Applications will be accepted on the standard application receipt dates as indicated in the application kit. The program announcement title and number must be typed on line 2a of the face page.

FIRST (R29) award applications must include at least three sealed letters of reference attached to the face page of the original application. FIRST award applications submitted without the required number of reference letters will be considered incomplete and will be returned without review.

The completed original application and five legible copies must be sent or delivered to:

Division of Research Grants
National Institutes of Health
Westwood Building, Room 240
Bethesda, MD 20892**

REVIEW CONSIDERATIONS

Applications will be assigned on the basis of established PHS referral guidelines. Applications will be reviewed for scientific and technical merit in accordance with the standard NIH peer review procedures. Following scientific-technical review, applications recommended for further consideration will receive a second-level review by the appropriate national advisory council.

AWARD CRITERIA

Applications will compete for available funds on the basis of scientific merit, program balance among research areas of the announcement, and the availability of funds.

INQUIRIES

Written and telephone inquiries concerning this PA are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues to:

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Direct inquiries regarding fiscal matters to:

Joanne Colbert
Grants and Contracts Management Office
National Institute on Aging
Gateway Building, Room 2N212
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AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.866. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410), as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR Part 52 and 45 CFR Parts 74 and 92. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or to the Health Systems Agency review. Awards will be administered under PHS grants policy as stated in the PHS Grants policy statement, DHHS Publication NO. (OASH) 90-50,000, revised October 1, 1990..

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